THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 40

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

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Ex parte DAVID A. CAMPBELL

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Appeal No. 94-3187
Application 07/939,556[1]

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ON BRIEF

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Before WILLIAM F. SMITH, SCHAFER and ELLIS, Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

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[1] Application for patent filed September 1, 1992. According to the appellant, this application is a continuation of Application 07/058,344, filed June 5, 1987, now abandoned; which is a division of Application 06/596,447, filed April 3, 1984, now U.S. Patent 4,693,893, issued September 15, 1987; which is a continuation of Application 06/565,648, filed December 27, 1983, now abandoned.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1, 4 through 9 and 12 through 15, all the claims in the application.

Claims 1, 6, 12 and 15 are illustrative of the subject matter on appeal and read as follows:

1. A genetically reassorted virus grown in cell culture in sufficient quantities to be useful for vaccine preparation without need of further multiplication, said virus being derived from an equine influenza virus and the human influenza virus A/Puerto Rico/8/34 which reassorted virus comprises RNA derived from the equine influenza virus coding for at least one neuraminidase or haemagglutinin surface antigen and the RNA segment derived from A/Puerto Rico/8/34 which codes for matrix protein.

6. A process for the preparation of a genetically reassorted virus comprising the steps of:

(a) allowing (i) equine influenza virus and (ii) the human influenza virus strain A/Puerto Rico/8/34 or a virus comprising the RNA 7 segment thereof to grow under conditions in which genetic reassortment can take place,

(b) selecting for genetically reassorted viruses having surface antigens from only the equine virus and having the RNA 7 segment derived from the A/Puerto Rico/8/34 virus, and

(c) growing those said reassortants from step (b) in cell culture.

12. A vaccine for equine influenza comprising an effective vaccination amount of attenuated genetically reassorted virus grown in cell culture and derrived [sic] from either or both of Eq1 and Eq2 equine influenza virus and the human influenza virus A/Puerto Rico/8/34, which reassorted virus comprises RNA derived from the equine influenza virus coding for at least one neuramidase or haemagglutinin surface antigen and an RNA segment derived from A/Puerto Rico/8/34, which codes for matrix protein in association

with a veterinary acceptable carrier which can contain an adjuvant suitable for use as vehicle to introduce the attenuated virus into the animal.

15. A method of vaccinating a horse against influenza by administration to the horse of an effective amount of (a) one, or (b) a primary followed by a secondary dosage with an interval of about 3 to about 7 weeks between doses of a genetically reassorted virus derived from equine influenza virus, attenuated and formulated with a veternary [sic] acceptable carrier which can contain an adjuvant as a vaccine according to claim 12.

The references relied upon by the examiner are:

Coggins et al. (Coggins) 4,683,137 July 28, 1987

Bosch et al. (Bosch), "RNA and Protein Synthesis in a Permissive and an Abortive Influenza Virus Infection," in “Negative Strand Viruses and the Host Cell,” eds. Mahy et al., Academic Press, pp. 465-473 (1978).

Baez et al. (Baez), "Gene Composition of High-Yielding Influenza Vaccine Strains Obtained by Recombination," The Journal of Infectious Diseases, vol. 141, pp. 362-365 (1980).

Brundage-Anguish et al. (Brundage-Anguish), "Live Temperature-Sensitive Equine Influenza Virus Vaccine: Generation of the Virus and Efficacy in Hamsters," Am. J. Vet. Res., vol. 43, pp. 869-874 (1982).

Claims 1, 4 through 9 and 12 through 15 stand rejected under 35 U.S.C. § 103 as unpatentable over either Coggins or Brundage-Anguish taken in view of Baez and Bosch.

We reverse.

BACKGROUND

The present invention is directed to genetically reassorted viruses derived from an equine influenza virus and the human influenza virus A/Puerto Rico/8/34 (PR8). The

reassorted virus contains RNA derived from the equine influenza virus coding for at least one neuraminidase or hemagglutinin surface antigen and the RNA segment from PR8 which codes for matrix protein. As set forth in the abstract of this application, appellant found that these reassortments will grow in cell culture even though the equine influenza virus used as a parent will not.

The ability of the present reassorted virus to grow in cell culture is discussed at page 3, lines 4-9, of the specification as follows:

> It has now surprisingly been found that if an equine influenza virus is genetically reassorted to produce a virus containing certain RNA derived from A/Puerto Rico/8/34, the genetically reassorted virus is able to grow in cell culture. There is no clear correlation between having a high yield in eggs and the ability to grow in cell culture, and there is no teaching in the prior art to suggest that a virus which grows well in eggs is likely to grow in cell culture.

and at page 4, lines 3-14, of the specification as follows:

> The involvement of matrix protein in general in virus growth in cell culture was suggested by Bosch et al, (in Negative Strand Viruses and the Host Cell (1978), Academic Press, edited by B. W. J. Mahy and others, page 465). However, this paper relates to the growth of fowl plague virus (FPV) and no mention is made of equine influenza virus. In view of the well known difficulty in making predictions about the behaviour of one type of influenza virus based on observations of another, this distinction is by no means trivial. See, for example Scholtissek et al, Virology (1977) 81 74-80, which illustrates the proposition that apparently small changes between influenza viruses have profound effects. This is amplified by

> Sweet and Smith (Microb. Revs. (1980) 44 (22), 303-30). Furthermore, there has been no suggestion that the segment in A/PR/8/34 coding for matrix protein is effective in conferring the ability to grow in cell culture.

As explained at page 3, lines 27-30, of the specification, it is important to understand that:

> Whereas it has been established by the applicants that the RNA segment which codes for matrix protein enables growth in cell culture to take place, it is not clear as to whether the matrix protein itself confers this ability: it may be some other gene product coded by the same RNA segment.

DISCUSSION

Assuming, without deciding, that the combined disclosures of Coggins, Brundage-Anguish and Baez would have suggested to one of ordinary skill in the art to form a genetically reassorted virus derived from an equine influenza virus and PR8 which comprises RNA derived from the equine influenza virus coding for at least one neuraminidase or hemagglutinin surface antigen and the RNA segment derived from PR8 which codes for matrix protein, that would not end the inquiry. Rather, a second determination would have to be made as to whether the applied prior art would have led one skilled in the art to reasonably expect that such a reassorted virus would grow in cell culture. For this aspect of the claimed invention, the examiner relies upon Bosch.

Bosch acknowledges in the abstract that many influenza virus infections of cells in culture do not result in the production of infectious virus. Bosch used Fowl Plague Virus

(FPV) to infect L cells and chick embryo fibroblasts. FPV infection of L cells resulted in low viral virus yields while the FPV infections of chick embryo fibroblasts resulted in relatively high virus yields. In order to define the factors responsible for these disparate results, Bosch compared the virus-specific RNA and protein synthesis of the two systems. The examiner relies upon Bosch's observation, set forth in the last full paragraph of page 467, that of the proteins analyzed in the chick embryo fibroblast and L cell cultures, the synthesis of matrix protein was reduced in the L cell culture. The examiner has inferred that the relatively higher production of matrix protein in the chick embryo fibroblast culture was responsible for the relatively higher virus yields obtained in that system. From this inference, the examiner concluded that one of ordinary skill in the art would have understood at the time of the present invention, from a consideration of all four of the applied references together, that a reassorted virus containing the RNA encoding matrix protein of PR8 would have expectedly been able to grow in high yields in cell culture. We disagree.

In our view, the narrow disclosure of Bosch does not support the sweeping conclusion reached by the examiner. Bosch initially indicates that many influenza virus infections of cells in culture do not result in the production of infectious virus. That teaching in and of itself provides evidence that the area in which appellant is working has a high degree of unpredictability. While infection of chick embryo fibroblasts resulted in relatively

high virus yields, Bosch, considered in its entirety, indicates to us that the results to be obtained from an influenza virus infection of cells in culture at the time of the present invention was unpredictable. This determination is consistent with appellant's characterization of the prior art at page 4, lines 3-14, of the specification referred to above.

When we consider the entire record, it is our view that one of ordinary skill in the art at the time of the present invention would not have reasonably expected that a reassorted virus derived from equine influenza virus and PR8 and containing the RNA's required by the claims on appeal would be capable of growing in cell culture.

The decision of the examiner is reversed.

REVERSED

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WILLIAM F. SMITH)

Administrative Patent Judge	)
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	) BOARD OF PATENT
RICHARD E. SCHAFER	)
Administrative Patent Judge	) APPEALS AND
	)
	) INTERFERENCES
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JOAN ELLIS	)
Administrative Patent Judge	)

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